IMMUNOLOGY
A SYNTHESIS
Second Edition

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PART-OPENING ELECTRON MICROGRAPHS

Part 1 (page 19): Antibody–hapten complex (purified rabbit anti-2,4-dinitrophenyl antibody and a bivalent hapten). [From Valentine and Green, 1967. *J. Mol. Biol.* 27: 615]

Part 2 (page 191): A resting lymphocyte, probably a T cell (×21,800). [Courtesy of D. Zucker-Franklin, New York University Medical Center]

Part 3 (page 543): Immune complexes, seen as electron-dense, hump-shaped deposits in the upper third of the photo, along a capillary wall in a glomerulus following streptococcal glomerulonephritis (×17,250). [Courtesy of M. N. Yum, Indiana University Medical Center]

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free hapten. In general, carriers are molecules that are of themselves immunogenic. Hence we may think of the hapten as an added determinant on an already immunogenic molecule. The study of hapten–carrier systems has given us much information about the nature of antigens and the antigen–antibody interaction, but it has also been one of the keys to understanding the cellular events in the immune response (see Chapter 17).

The Specificity of Serological Reactions

Landsteiner studied haptens and carriers in an attempt to work out the rules that govern antigenicity. The compilation of these studies appeared in his classic treatise, *The Specificity of Serological Reactions*. As we will see, no universal rules governing antigenicity came out of this work, but what did emerge was the realization that the chemical properties of the antigen molecule determine the specificity of the immune system. SPECIFICITY is defined as the ability of antibodies produced in response to an antigen to react with that antigen and not with others. The thoroughness of Landsteiner's approach and the elegance of his thought make browsing in this volume, which is available in paperback, a worthwhile experience for any scientist.

Landsteiner immunized a rabbit with a hapten–carrier conjugate. This injection resulted in antiserum with both anti-hapten and anti-carrier activity. He then conjugated the hapten to a different carrier and reacted the conjugate with the same antiserum to test for the presence of *anti-hapten* antibodies. Because he had changed carrier molecules for the test, there was no anti-carrier reaction; the reaction observed was between the anti-hapten antibodies and the hapten. He then varied the properties of the hapten in order to study, for example, the effect of acidic or ionic groups on the ability of the antibody raised against the original hapten to react with the modified hapten. Although no general rules emerged, it is instructive to look at some of Landsteiner's conclusions (Landsteiner, 1962):

> The principal results of numerous precipitin tests with azoproteins were the following . . .
>
> 1. First of all, the nature of the acidic groups was of decisive influence. [p. 163]

Data from Landsteiner's experiments are shown in Tables 1–4. Antibody is raised against aminobenzene or aminobenzene with

Cross Reactivity

Antibody molecules can exhibit great specificity, but there are CROSS REACTIONS—cases in which antibody to antigen A also reacts with antigen B. This can be due to the presence of the same molecular configuration, or ANTIGENIC DETERMINANT, on the two antigens, or to properties of a determinant that allow it to be recognized as though it were another group. Antigenic determinants are also called *epitopes*. As we move through the book we will use these terms almost interchangeably. We can conceive of molecules that have similar but not identical structures and appear in closely related species. These molecules may have enough similarity to allow antibodies against one to react with the other.[1]

Table 5 shows the percentage of cross reactivity between albumins of different species. Antibody was made against bovine serum albumin (BSA), and the extent of the ability of albumins from other species to react with the anti-BSA was then determined. This cross reactivity is probably due to the presence of common determinants on the different albumins. To determine this, however, each of the determinants must be isolated and studied chemically. Even then, as we will see later in this chapter, we cannot be quite certain of

[1] The neurobiologist A. K. Hall has suggested the term IMMUNOFREQUENT for such determinants.

Table 5 Cross reaction between BSA and other albumins.[a]

Albumin source	Percentage of cross reactivity with BSA	Albumin source	Percentage of cross reactivity with BSA
Human	15	Mouse	10
Pig	32	Rat	13
Sheep	75	Hamster	13
Horse	13	Cat	25
Guinea pig	5	Vallaroo	5
Dog	13		

Source: Data from Weigle, 1961. *J. Immunol.* 87: 599.

[a] Rabbit anti-BSA was absorbed with each of the albumins listed and then tested for its ability to react with BSA. This ability is expressed as a percentage *cross reactivity*. The data show that sheep BSA has the highest amount of cross reactivity and guinea pig and vallaroo the least.